NMCP COVID-19 Literature Report #58: Friday, 05 February 2021

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Purpose: These weekly reports, published on Fridays, are curated collections of current research, evidence reviews, special reports, grey literature, and news regarding the COVID-19 pandemic that may be of interest to medical providers, leadership, and decision makers.

All reports are available online at https://nmcp.libguides.com/covidreport. Access is private; you will need to use the direct link or bookmark the URL, along with the case-sensitive password "NMCPfinest".

Disclaimer: I am not a medical professional. This document is current as of the date noted above. While I make every effort to find and summarize available data, I cannot cover everything in the literature on COVID-19. Please feel free to reach out with questions, suggestions for future topics, or any other feedback.

Statistics

Global today: 105,006,686 confirmed cases and 2,287,129 deaths in 192 countries/regions

29 JAN 2021: 101,605,084 confirmed cases and 2,194,204 deaths in 192 countries/regions

22 JAN 2021: 97,645,892 confirmed cases and 2,094,191 deaths in 191 countries/regions

*United States** top 5 states by cases

	TOTAL US	CA	TX	FL	NY	IL
Cases	26,680,536	3,382,932	2,463,967	1,752,330	1,450,912	1,137,559
Deaths	455,882	44,298	38,453	27,247	44,298	21,497

*see census.gov for current US Population data; NA: not all data available JHU CSSE as of 1000 EDT 05 February 2021

Virginia is ranked 17th in cases and 22nd in deaths.

Virginia	Total (state)	Chesapeake	Hampton	Newport News	Norfolk	Portsmouth	Suffolk	Virginia Beach
Cases	521,467	16,126	7,559	10,102	13,897	6,832	6,096	27,272
Hospitalizations	21,893	761	240	266	725	502	317	1,113
Deaths	6,732	141	68	103	148	99	115	225

VA DOH as of 1000 EDT 05 February 2021

Special Reports

NIH: COVID-19 Treatment Guidelines (updated 03 February 2021)

The COVID-19 Treatment Guidelines Panel's Statement on the Use of Tocilizumab (and Other Interleukin-6 Inhibitors) for the Treatment of COVID-19

"Based on the available evidence, the Panel has determined the following:

- For patients who are within 24 hours of admission to the ICU and who require invasive or noninvasive mechanical ventilation or high-flow oxygen (>0.4 FiO2/30 L/min of oxygen flow), there are insufficient data to recommend either for or against the use of tocilizumab or sarilumab for the treatment of COVID-19.
    - Although many trials of tocilizumab for the treatment of COVID-19 have included patients who meet the above criteria, the collective data available to date preclude a definitive recommendation for or against the use of the drug.
    - In view of the results from the REMAP-CAP trial (described below), some Panel members would administer a single dose of tocilizumab (8 mg/kg of actual body weight, up to 800 mg) in addition to dexamethasone to patients who meet the above criteria and who are also exhibiting rapid progression of respiratory failure.
    - Too few patients in REMAP-CAP received sarilumab for the Panel to assess its efficacy in the treatment of patients who met the above criteria.
- For patients who do not require ICU-level care or who are admitted to the ICU but do not meet the above criteria, the Panel recommends against the use of tocilizumab or sarilumab for the treatment of COVID-19, except in a clinical trial (BIIa)."

GAO: COVID-19: Critical Vaccine Distribution, Supply Chain, Program Integrity, and Other Challenges Require Focused Federal Attention (28 January 2021)

"This review of the federal response to the COVID-19 pandemic is our fifth comprehensive report since June 2020 about the implementation of the CARES Act.

We remain deeply troubled by the lack of sufficient federal action on critical gaps identified and by the lack of clear plans to address these gaps. For example, a clear and comprehensive vaccine distribution plan remains a work in progress.

As of January, 27 of our 31 previous recommendations had not been implemented. This report makes 13 new recommendations to improve agencies' public health and economic recovery efforts, including the development of a national testing strategy."

ACOG: Vaccinating Pregnant and Lactating Patients Against COVID-19 (updated 27 January 2021)

The updated guidance says in part:

"COVID-19 vaccine development and regulatory approval are rapidly progressing. Thus, information and recommendations will evolve as more data are collected about these vaccines and their use in specific populations. This Practice Advisory is intended to be an overview of currently available COVID-19 vaccines and guidance for their use in pregnant and lactating patients. The U.S. Food and Drug Administration (FDA) issued an Emergency Use Authorization (EUA) for the following vaccines:

- Pfizer-BioNtech mRNA vaccine (BNT162b2): for use in individuals age 16 years and older as a 2-dose regimen given 3 weeks (21 days) apart.
- Moderna mRNA-1273 vaccine: for use in individuals age 18 and older as a 2-dose regimen given 1 month (28 days) apart.

After an explicit, evidence-based review of all available data, the Advisory Committee on Immunization Practices (ACIP) issued interim recommendations for use of the Pfizer-BioNTech COVID-19 vaccine in persons aged ≥16 years for the prevention of COVID-19 (CDC 2020) and the use of the Moderna-1273 COVID-19 vaccine in persons aged ≥ 18 years (CDC 2020).

ACOG recommends that COVID-19 vaccines should not be withheld from pregnant individuals who meet criteria for vaccination based on ACIP-recommended priority groups.

COVID-19 vaccines should be offered to lactating individuals similar to non-lactating individuals when they meet criteria for receipt of the vaccine based on prioritization groups outlined by the ACIP.

Individuals considering a COVID-19 vaccine should have access to available information about the safety and efficacy of the vaccine, including information about data that are not available. A conversation between the patient and their clinical team may assist with decisions regarding the use of vaccines approved under EUA for the prevention of COVID-19 by pregnant patients. Important considerations include:

- the level of activity of the virus in the community
- the potential efficacy of the vaccine
- the risk and potential severity of maternal disease, including the effects of disease on the fetus and newborn
- the safety of the vaccine for the pregnant patient and the fetus.

While a conversation with a clinician may be helpful, it should not be required prior to vaccination, as this may cause unnecessary barriers to access."

Selected Literature: Peer-Reviewed Journals

Date given is the date published or posted online; often these papers are ahead of print.

05 February 2021

MMWR: Racial and Ethnic Disparities in the Prevalence of Stress and Worry, Mental Health Conditions, and Increased Substance Use Among Adults During the COVID-19 Pandemic — United States, April and May 2020

> "What is already known about this topic? Racial and ethnic minority groups have experienced disparities in mental health and substance misuse related to access to care, psychosocial stress, and social determinants of health.
>
> What is added by this report? Combined prevalence estimates of current depression, initiating or increasing substance use, and suicidal thoughts/ideation among U.S. adults aged ≥18 years were 28.6%, 18.2%, and 8.4%, respectively. Hispanic adults reported a higher prevalence of psychosocial stress related to not having enough food or stable housing than did adults in other racial and ethnic groups.
>
> What are the implications for public health practice? Addressing psychosocial stressors, mental health conditions, and substance misuse among U.S. adults during the COVID-19 pandemic is important, as are interventions tailored for racial and ethnic minority groups."

MMWR: Sexual Orientation Disparities in Risk Factors for Adverse COVID-19–Related Outcomes, by Race/Ethnicity — Behavioral Risk Factor Surveillance System, United States, 2017–2019

> "What is already known about this topic? Risks for COVID-19 acquisition and severe associated illness vary by characteristics, including race/ethnicity, age, and urban/rural residence. U.S. COVID-19 surveillance systems lack information on sexual orientation, hampering examination of COVID-19–associated disparities among sexual minority adults.
>
> What is added by this report? Sexual minority persons in the United States have higher self-reported prevalences of several underlying health conditions associated with severe outcomes from COVID-19 than do heterosexual persons, both in the overall population and among racial/ethnic minority groups.
>
> What are the implications for public health practice? Inclusion of sexual orientation and gender identity data in COVID-19 surveillance and other data collections could improve knowledge about disparities in infections and adverse outcomes among sexual and gender minority populations, overall and by race/ethnicity."

MMWR: Decreases in Young Children Who Received Blood Lead Level Testing During COVID-19 — 34 Jurisdictions, January–May 2020

> "What is already known about this topic? Lead can affect a young child's ability to learn and cause other adverse health effects; no safe blood lead level (BLL) is known. Routine testing can detect elevated BLLs.
>
> What is added by this report? During January–May 2020, 34% fewer U.S. children had BLL testing compared with those during January–May 2019, with an estimated 9,603 children with elevated BLLs missed. All 34 reporting jurisdictions reported that fewer children were tested following the COVID-19 national emergency declaration in March.
>
> What are the implications for public health practice? COVID-19 has adversely affected identification of children with elevated BLLs, exposure elimination, and linkage to services. It remains important that providers ensure that young children receive appropriate lead testing and care management."

04 February 2021

CMAJ: COVID-19 in patients undergoing long-term dialysis in Ontario

> "Patients undergoing longterm dialysis may be at higher risk of infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and of associated disease and mortality. We aimed to describe the incidence, risk factors and outcomes for infection in these patients in Ontario, Canada.
>
> We used linked data sets to compare disease characteristics and mortality between patients receiving longterm dialysis in Ontario who were diagnosed SARS-CoV-2 positive and those who did not acquire SARS-CoV-2 infection, between Mar. 12 and Aug. 20, 2020. We collected data on SARS-CoV-2 infection prospectively. We evaluated risk factors for infection and death using multivariable logistic regression analyses.
>
> During the study period, 187 (1.5%) of 12 501 patients undergoing dialysis were diagnosed with SARS-CoV-2 infection. Of those with SARS-CoV-2 infection, 117 (62.6%) were admitted to hospital and the case fatality rate was 28.3%. Significant predictors of infection included in-centre hemodialysis versus home dialysis (odds ratio [OR] 2.54, 95% confidence interval [CI] 1.59–4.05), living in a long-term care residence (OR 7.67, 95% CI 5.30–11.11), living in the Greater Toronto Area (OR 3.27, 95% CI 2.21–4.80), Black ethnicity (OR 3.05, 95% CI 1.95–4.77), Indian subcontinent ethnicity (OR 1.70, 95% CI 1.02–2.81), other non-White ethnicities (OR 2.03, 95% CI 1.38–2.97) and lower income quintiles (OR 1.82, 95% CI 1.15–2.89).

Patients undergoing long-term dialysis are at increased risk of SARS-CoV-2 infection and death from coronavirus disease 2019. Special attention should be paid to addressing risk factors for infection, and these patients should be prioritized for vaccination."

03 February 2021

JAMA Psychiatry: Trends in US Emergency Department Visits for Mental Health, Overdose, and Violence Outcomes Before and During the COVID-19 Pandemic

"Question: Did US emergency department (ED) visits for mental health, suicide attempts, overdose, and violence outcomes change during the coronavirus disease 2019 (COVID-19) pandemic?

Findings: This cross-sectional study of almost 190 million ED visits found that visit rates for mental health conditions, suicide attempts, all drug and opioid overdoses, intimate partner violence, and child abuse and neglect were higher in mid-March through October 2020, during the COVID-19 pandemic, compared with the same period in 2019.

Meaning: These findings suggest that ED use and priorities for care seeking shifted during the COVID-19 pandemic, underscoring mental health, substance use, and violence risk screening and prevention needs during public health crises."

Nat Metab: SARS-CoV-2 infects and replicates in cells of the human endocrine and exocrine pancreas

"Infection-related diabetes can arise as a result of virus-associated β-cell destruction. Clinical data suggest that the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), causing the coronavirus disease 2019 (COVID-19), impairs glucose homoeostasis, but experimental evidence that SARS-CoV-2 can infect pancreatic tissue has been lacking. In the present study, we show that SARS-CoV-2 infects cells of the human exocrine and endocrine pancreas ex vivo and in vivo. We demonstrate that human β-cells express viral entry proteins, and SARS-CoV-2 infects and replicates in cultured human islets. Infection is associated with morphological, transcriptional and functional changes, including reduced numbers of insulin-secretory granules in β-cells and impaired glucose-stimulated insulin secretion. In COVID-19 full-body postmortem examinations, we detected SARS-CoV-2 nucleocapsid protein in pancreatic exocrine cells, and in cells that stain positive for the β-cell marker NKX6.1 and are in close proximity to the islets of Langerhans in all four patients investigated. Our data identify the human pancreas as a target of SARS-CoV-2 infection and suggest that β-cell infection could contribute to the metabolic dysregulation observed in patients with COVID-19."

PNAS: Mechanistic transmission modeling of COVID-19 on the Diamond Princess cruise ship demonstrates the importance of aerosol transmission

> "We find that airborne transmission likely accounted for >50% of disease transmission on the *Diamond Princess* cruise ship, which includes inhalation of aerosols during close contact as well as longer range. These findings underscore the importance of implementing public health measures that target the control of inhalation of aerosols in addition to ongoing measures targeting control of large-droplet and fomite transmission, not only aboard cruise ships but in other indoor environments as well. Guidance from health organizations should include a greater emphasis on controls for reducing spread by airborne transmission. Last, although our work is based on a cruise ship outbreak of COVID-19, the model approach can be applied to other indoor environments and other infectious diseases."

02 February 2021

Emerg Infect Dis: SARS-CoV-2 seropositivity among US Marine recruits attending basic training, United States, spring–fall 2020

> " In a study of US Marine recruits, seroprevalence of severe acute respiratory syndrome coronavirus 2 IgG was 9.0%. Hispanic and non-Hispanic Black participants and participants from states affected earlier in the pandemic had higher seropositivity rates. These results suggest the need for targeted public health strategies among young adults at increased risk for infection."

Intensive Care Med: Extracorporeal membrane oxygenation in patients with severe respiratory failure from COVID-19

> "Limited data are available on venovenous extracorporeal membrane oxygenation (ECMO) in patients with severe hypoxemic respiratory failure from coronavirus disease 2019 (COVID-19).
>
> We examined the clinical features and outcomes of 190 patients treated with ECMO within 14 days of ICU admission, using data from a multicenter cohort study of 5122 critically ill adults with COVID-19 admitted to 68 hospitals across the United States. To estimate the effect of ECMO on mortality, we emulated a target trial of ECMO receipt versus no ECMO receipt within 7 days of ICU admission among mechanically ventilated patients with severe hypoxemia (PaO2/FiO2 < 100). Patients were followed until hospital discharge, death, or a minimum of 60 days. We adjusted for confounding using a multivariable Cox model.
>
> Among the 190 patients treated with ECMO, the median age was 49 years (IQR 41–58), 137 (72.1%) were men, and the median PaO2/FiO2 prior to ECMO initiation was 72 (IQR 61–90). At 60 days, 63 patients (33.2%) had died, 94 (49.5%) were discharged, and 33 (17.4%)

remained hospitalized. Among the 1297 patients eligible for the target trial emulation, 45 of the 130 (34.6%) who received ECMO died, and 553 of the 1167 (47.4%) who did not receive ECMO died. In the primary analysis, patients who received ECMO had lower mortality than those who did not (HR 0.55; 95% CI 0.41–0.74). Results were similar in a secondary analysis limited to patients with PaO2/FiO2 < 80 (HR 0.55; 95% CI 0.40–0.77).

In select patients with severe respiratory failure from COVID-19, ECMO may reduce mortality."

JAMA: Asymptomatic SARS-CoV-2 Infections Among Persons Entering China From April 16 to October 12, 2020

"This population epidemiology study characterizes trends in the prevalence of asymptomatic severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection among international entrants testing positive for SARS-CoV-2 at Chinese border checkpoints between mid-April and mid-October 2020."

Lancet: Safety and efficacy of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine: an interim analysis of a randomised controlled phase 3 trial in Russia

"A heterologous recombinant adenovirus (rAd)-based vaccine, Gam-COVID-Vac (Sputnik V), showed a good safety profile and induced strong humoral and cellular immune responses in participants in phase 1/2 clinical trials. Here, we report preliminary results on the efficacy and safety of Gam-COVID-Vac from the interim analysis of this phase 3 trial.

We did a randomised, double-blind, placebo-controlled, phase 3 trial at 25 hospitals and polyclinics in Moscow, Russia. We included participants aged at least 18 years, with negative SARS-CoV-2 PCR and IgG and IgM tests, no infectious diseases in the 14 days before enrolment, and no other vaccinations in the 30 days before enrolment. Participants were randomly assigned (3:1) to receive vaccine or placebo, with stratification by age group. Investigators, participants, and all study staff were masked to group assignment. The vaccine was administered (0·5 mL/dose) intramuscularly in a prime-boost regimen: a 21-day interval between the first dose (rAd26) and the second dose (rAd5), both vectors carrying the gene for the full-length SARS-CoV-2 glycoprotein S. The primary outcome was the proportion of participants with PCR-confirmed COVID-19 from day 21 after receiving the first dose. All analyses excluded participants with protocol violations: the primary outcome was assessed in participants who had received two doses of vaccine or placebo, serious adverse events were assessed in all participants who had received at least one dose at the time of database lock, and rare adverse events were assessed in all participants who had received two doses and for whom all available data were verified in the case report form at the time of database lock. The trial is registered at ClinicalTrials.gov (NCT04530396).

Between Sept 7 and Nov 24, 2020, 21 977 adults were randomly assigned to the vaccine group (n=16 501) or the placebo group (n=5476). 19 866 received two doses of vaccine or placebo and were included in the primary outcome analysis. From 21 days after the first dose of vaccine (the day of dose 2), 16 (0·1%) of 14 964 participants in the vaccine group and 62 (1·3%) of 4902 in the placebo group were confirmed to have COVID-19; vaccine efficacy was 91·6% (95% CI 85·6–95·2). Most reported adverse events were grade 1 (7485 [94·0%] of 7966 total events). 45 (0·3%) of 16 427 participants in the vaccine group and 23 (0·4%) of 5435 participants in the placebo group had serious adverse events; none were considered associated with vaccination, with confirmation from the independent data monitoring committee. Four deaths were reported during the study (three [<0·1%] of 16 427 participants in the vaccine group and one [<0·1%] of 5435 participants in the placebo group), none of which were considered related to the vaccine.

This interim analysis of the phase 3 trial of Gam-COVID-Vac showed 91·6% efficacy against COVID-19 and was well tolerated in a large cohort."

Lancet Infect Dis: Transmission of COVID-19 in 282 clusters in Catalonia, Spain: a cohort study

"We analysed data from a large cluster-randomised clinical trial on post-exposure therapy for COVID-19 that provided new information on SARS-CoV-2 transmission dynamics. Several design components add value to this dataset. Notably, quantitative PCR was available for the index cases to estimate risk of transmission. Additionally, quantitative PCR was also done on asymptomatic contacts at the time of enrolment allowing us to investigate the dynamics of symptomatic disease onset among them. We found that the viral load of the index case was the leading determinant of the risk of SARS-CoV-2 PCR positivity among contacts. Among contacts who were SARS-CoV-2 PCR positive at baseline, viral load significantly influenced the risk of developing the symptomatic disease in a dose-dependent manner. This influence also became apparent in the incubation time, which shortened with increasing baseline viral loads.

Our results provide important insights into the knowledge regarding the risk of SARS-CoV-2 transmission and COVID-19 development. The fact that the transmission risk was primarily driven by the viral load of index cases, more than other factors such as their symptoms or age, suggests that all cases should be considered potential transmitters irrespective of their presentation and encourages the assessment of viral load in patients with a larger number of close contacts. Similarly, our results regarding the risk and expected time to developing symptomatic COVID-19 encourage risk stratification of newly diagnosed SARS-CoV-2 infections on the basis of the initial viral load."

PLoS One: Ethics of emerging infectious disease outbreak responses: Using Ebola virus disease as a case study of limited resource allocation

"Emerging infectious diseases such as Ebola Virus Disease (EVD), Nipah Virus Encephalitis and Lassa fever pose significant epidemic threats. Responses to emerging infectious disease outbreaks frequently occur in resource-constrained regions and under high pressure to quickly contain the outbreak prior to potential spread. As seen in the 2020 EVD outbreaks in the Democratic Republic of Congo and the current COVID-19 pandemic, there is a continued need to evaluate and address the ethical challenges that arise in the high stakes environment of an emerging infectious disease outbreak response. The research presented here provides analysis of the ethical challenges with regard to allocation of limited resources, particularly experimental therapeutics, using the 2013–2016 EVD outbreak in West Africa as a case study. In-depth semi-structured interviews were conducted with senior healthcare personnel (n = 16) from international humanitarian aid organizations intimately engaged in the 2013–2016 EVD outbreak response in West Africa. Interviews were recorded in private setting, transcribed, and iteratively coded using grounded theory methodology. A majority of respondents indicated a clear propensity to adopt an ethical framework of guiding principles for international responses to emerging infectious disease outbreaks. Respondents agreed that prioritization of frontline workers' access to experimental therapeutics was warranted based on a principle of reciprocity. There was widespread acceptance of adaptive trial designs and greater trial transparency in providing access to experimental therapeutics. Many respondents also emphasized the importance of community engagement in limited resource allocation scheme design and culturally appropriate informed consent procedures. The study results inform a potential ethical framework of guiding principles based on the interview participants' insights to be adopted by international response organizations and their healthcare workers in the face of allocating limited resources such as experimental therapeutics in future emerging infectious disease outbreaks to ease the moral burden of individual healthcare providers."

Science: Age groups that sustain resurging COVID-19 epidemics in the United States

"Following initial declines, in mid 2020 a resurgence in transmission of novel coronavirus disease (COVID-19) occurred in the US and Europe. As COVID19 disease control efforts are re-intensified, understanding the age demographics driving transmission and how these affect the loosening of interventions is crucial. We analyze aggregated, age-specific mobility trends from more than 10 million individuals in the US and link these mechanistically to age-specific COVID-19 mortality data. We estimate that as of October 2020, individuals aged 20-49 are the only age groups sustaining resurgent SARS-CoV-2 transmission with reproduction numbers well above one, and that at least 65 of 100 COVID-19 infections originate from individuals aged 20-49 in the US. Targeting interventions – including transmission-blocking vaccines – to adults aged 20-49 is an important consideration in halting resurgent epidemics and preventing COVID-19-attributable deaths."

01 February 2021

Am J Psychiatry: Anxiety Levels Among Physician Mothers During the COVID-19 Pandemic

> Letter to the editor: "Of 1,809 participants, 41% scored above the cutoff points for moderate or severe anxiety as measured by the GAD-7, with 18% reporting severe anxiety. The median GAD-7 score was 8.0 (interquartile range=6.0–13.0). Multivariable analysis revealed that anxiety was higher among frontline workers than among those who were not frontline workers (46% compared with 37%, respectively; β=0.80, p=0.01) and informal caregivers (β=0.873, p=0.02) and lower among Asian respondents (β=−1.1, p<0.004). No other key demographic variables were associated with differences in anxiety levels.
>
> In summary, rates of anxiety among physician mothers in this study appear substantial; for context, in the general U.S. population in normal circumstances, about 19% of adults had any anxiety disorder in the past year."

Anaesthesia: Mortality in patients admitted to intensive care with COVID-19: an updated systematic review and meta-analysis of observational studies

> "The COVID-19 pandemic continues to cause critical illness and deaths internationally. Up to 31 May 2020, mortality in patients admitted to intensive care units (ICU) with COVID-19 was 41.6%. Since then, changes in therapeutics and management may have improved outcomes. Also, data from countries affected later in the pandemic are now available. We searched MEDLINE, Embase, PubMed and Cochrane databases up to 30 September 2020 for studies reporting ICU mortality among adult patients with COVID-19 and present an updated systematic review and meta-analysis. The primary outcome measure was death in intensive care as a proportion of completed ICU admissions, either through discharge from intensive care or death. We identified 52 observational studies including 43,128 patients, and first reports from the Middle East, South Asia and Australasia, as well as four national or regional registries. Reported mortality was lower in registries compared with other reports. In two regions, mortality differed significantly from all others, being higher in the Middle East and lower in a single registry study from Australasia. Although ICU mortality (95%CI) was lower than reported in June (35.5% (31.3–39.9%) vs. 41.6% (34.0–49.7%)), the absence of patient-level data prevents a definitive evaluation. A lack of standardisation of reporting prevents comparison of cohorts in terms of underlying risk, severity of illness or outcomes. We found that the decrease in ICU mortality from COVID-19 has reduced or plateaued since May 2020 and note the possibility of some geographical variation. More standardisation in reporting would improve the ability to compare outcomes from different reports."

Health Aff: COVID-19 Through The Eyes Of A Black Medical Student

> "In the face of the racial health disparities made more visible during the COVID-19 pandemic, statistics tell only part of the story."

JAMA: Association of Intravenous Immunoglobulins Plus Methylprednisolone vs Immunoglobulins Alone With Course of Fever in Multisystem Inflammatory Syndrome in Children

> "Question: Is there an association between treatment with intravenous immunoglobulins (IVIG) plus methylprednisolone vs IVIG alone and course of fever in multisystem inflammatory syndrome in children (MIS-C) associated with severe acute respiratory syndrome coronavirus 2?
>
> Findings: This retrospective cohort study included 111 children with MIS-C. After propensity score matching, the rate of treatment failure (defined by the persistence of fever 2 days after the introduction of first-line therapy or recrudescence of fever within 7 days) for those who received IVIG plus methylprednisolone vs IVIGs alone was 9% vs 51%, a difference that was statistically significant.
>
> Meaning: Combined treatment with methylprednisolone vs IVIG alone was associated with a better course of fever in MIS-C."

MMWR: Demographic Characteristics of Persons Vaccinated During the First Month of the COVID-19 Vaccination Program — United States, December 14, 2020–January 14, 2021

> "What is already known about this topic? In December 2020, two COVID-19 vaccines were authorized for emergency use in the United States. The first groups prioritized for vaccination included health care personnel and long-term care facility residents.
>
> What is added by this report? During the first month of the U.S. COVID-19 vaccination program, approximately 13,000,000 persons received ≥1 dose of vaccine. Among persons with demographic data, 63.0% were women, 55.0% were aged ≥50 years, and 60.4% were non-Hispanic White.
>
> What are the implications for public health practice? As the vaccination program expands, it is critical to ensure efficient and equitable administration to persons in each successive vaccine priority category, especially those at highest risk for infection and severe health outcomes."

30 January 2021

Clin Infect Dis: COVID-19 symptoms and SARS-CoV-2 antibody positivity in a large survey of first responders and healthcare personnel, May-July 2020

> "A SARS-CoV-2 serosurvey among first responder/healthcare personnel showed that loss of taste/smell was most predictive of seropositivity; percent seropositivity increased with number of COVID-19 symptoms. However, 22.9% with nine symptoms were seronegative,

and 8.3% with no symptoms were seropositive. These findings demonstrate limitations of symptom-based surveillance and importance of testing."

Clin Infect Dis: The impact of vaccination on COVID-19 outbreaks in the United States

"Global vaccine development efforts have been accelerated in response to the devastating COVID-19 pandemic. We evaluated the impact of a 2-dose COVID-19 vaccination campaign on reducing incidence, hospitalizations, and deaths in the United States (US).

We developed an agent-based model of SARS-CoV-2 transmission and parameterized it with US demographics and age-specific COVID-19 outcomes. Healthcare workers and high-risk individuals were prioritized for vaccination, while children under 18 years of age were not vaccinated. We considered a vaccine efficacy of 95% against disease following 2 doses administered 21 days apart achieving 40% vaccine coverage of the overall population within 284 days. We varied vaccine efficacy against infection, and specified 10% pre-existing population immunity for the base-case scenario. The model was calibrated to an effective reproduction number of 1.2, accounting for current non-pharmaceutical interventions in the US.

Vaccination reduced the overall attack rate to 4.6% (95% CrI: 4.3% - 5.0%) from 9.0% (95% CrI: 8.4% - 9.4%) without vaccination, over 300 days. The highest relative reduction (54-62%) was observed among individuals aged 65 and older. Vaccination markedly reduced adverse outcomes, with non-ICU hospitalizations, ICU hospitalizations, and deaths decreasing by 63.5% (95% CrI: 60.3% - 66.7%), 65.6% (95% CrI: 62.2% - 68.6%), and 69.3% (95% CrI: 65.5% - 73.1%), respectively, across the same period.

Our results indicate that vaccination can have a substantial impact on mitigating COVID-19 outbreaks, even with limited protection against infection. However, continued compliance with non-pharmaceutical interventions is essential to achieve this impact."

Lancet: Estimating the health impact of vaccination against ten pathogens in 98 low-income and middle-income countries from 2000 to 2030: a modelling study

"The current study advances previous work in terms of scale (number of countries, number of pathogens, and time period), in its emphasis on standardising model inputs (vaccine coverage and demography) and outputs (mortality and disability-adjusted life-years averted), and in assessing uncertainty in estimates of vaccine impact. Standardisation allowed impacts to be combined across and compared between vaccines. Uncertainty was assessed via probabilistic sensitivity analysis and by combining outputs from multiple models for each disease.

Rigorous estimates of the impact of childhood vaccination programmes on morbidity and mortality inform public health investment decisions made by countries and global donors. The results highlight the importance of maintaining and increasing vaccine coverage to

sustain gains made in reducing infectious disease-related mortality in LMICs [low-income and middle-income countries]."

29 January 2021

Ann Intern Med: Quantification of Occupational and Community Risk Factors for SARS-CoV-2 Seropositivity Among Health Care Workers in a Large U.S. Health Care System

"Identifying occupational risk factors for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection among health care workers (HCWs) can improve HCW and patient safety.

A logistic regression model was fitted to data from a cross-sectional survey conducted in April to June 2020, linking risk factors for occupational and community exposure to coronavirus disease 2019 (COVID-19) with SARS-CoV-2 seropositivity.

Employees and medical staff members elected to participate in SARS-CoV-2 serology testing offered to all HCWs as part of a quality initiative and completed a survey on exposure to COVID-19 and use of personal protective equipment.

Demographic risk factors for COVID-19, residential ZIP code incidence of COVID-19, occupational exposure to HCWs or patients who tested positive on polymerase chain reaction test, and use of personal protective equipment as potential risk factors for infection. The outcome was SARS-CoV-2 seropositivity.

Adjusted SARS-CoV-2 seropositivity was estimated to be 3.8% (95% CI, 3.4%-4.3%) (positive, n = 582) among the 10 275 HCWs (35% of the Emory Healthcare workforce) who participated in the survey. Community contact with a person known or suspected to have COVID-19 (adjusted odds ratio [aOR], 1.9 [CI, 1.4 to 2.6]; 77 positive persons [10.3%]) and community COVID-19 incidence (aOR, 1.5 [CI, 1.0 to 2.2]) increased the odds of infection. Black individuals were at high risk (aOR, 2.1 [CI, 1.7 to 2.6]; 238 positive persons [8.3%]).

Participation rates were modest and key workplace exposures, including job and infection prevention practices, changed rapidly in the early phases of the pandemic.

Demographic and community risk factors, including contact with a COVID-19–positive person and Black race, are more strongly associated with SARS-CoV-2 seropositivity among HCWs than is exposure in the workplace."

Ann Noninvasive Electrocardiol: The value of ECG changes in risk stratification of COVID-19 patients

"We evaluated 269 consecutive patients admitted to our center with confirmed SARS-CoV-2 infection. ECGs available at admission and after 1 week from hospitalization were assessed.

We evaluated the correlation between ECGs findings and major adverse events (MAE) as the composite of intra-hospital all-cause mortality or need for invasive mechanical ventilation. Abnormal ECGs were defined if primary ST-T segment alterations, left ventricular hypertrophy, tachy or bradyarrhythmias and any new AV, bundle blocks or significant morphology alterations (e.g., new Q pathological waves) were present.

Abnormal ECG at admission (106/216) and elevated baseline troponin values were more common in patients who developed MAE (p = .04 and p = .02, respectively). Concerning ECGs recorded after 7 days (159), abnormal findings were reported in 53.5% of patients and they were more frequent in those with MAE (p = .001). Among abnormal ECGs, ischemic alterations and left ventricular hypertrophy were significantly associated with a higher MAE rate. The multivariable analysis showed that the presence of abnormal ECG at 7 days of hospitalization was an independent predictor of MAE (HR 3.2; 95% CI 1.2–8.7; p = .02). Furthermore, patients with abnormal ECG at 7 days more often required transfer to the intensive care unit (p = .01) or renal replacement therapy (p = .04).

Patients with COVID-19 should receive ECG at admission but also during their hospital stay. Indeed, electrocardiographic alterations during hospitalization are associated with MAE and infection severity."

JAMA Netw Open: Association Between Receipt of Unemployment Insurance and Food Insecurity Among People Who Lost Employment During the COVID-19 Pandemic in the United States

"Question: Was the receipt of unemployment insurance and a $600/wk federal supplement to unemployment insurance associated with reduced food insecurity among people in low- and middle-income households who lost work during the coronavirus disease 2019 (COVID-19) pandemic?

Findings: In this cohort study of 1119 adults who lost work during the COVID-19 pandemic, unemployment insurance was associated with a 35% relative decline in food insecurity and a 48% relative decline in eating less due to financial constraints. The $600/wk federal supplement was associated with additional reductions in food insecurity.

Meaning: These findings suggest that expanding the amount and duration of unemployment insurance may be an effective approach to reducing food insecurity."

JAMA Netw Open: Association of Social and Demographic Factors With COVID-19 Incidence and Death Rates in the US

"Question: Are population-level social factors associated with coronavirus disease 2019 (COVID-19) incidence and mortality?

Findings: In this cross-sectional study including 4 289 283 COVID-19 cases and 147 074 COVID-19 deaths, county-level sociodemographic risk factors as assessed by the Social Vulnerability Index were associated with greater COVID-19 incidence and mortality.

Meaning: These findings suggest that to address inequities in the burden of the COVID-19 pandemic, these sociodemographic risk factors and their root causes must be addressed."

Lancet: Safety and immunogenicity of S-Trimer (SCB-2019), a protein subunit vaccine candidate for COVID-19 in healthy adults: a phase 1, randomised, double-blind, placebo-controlled trial

"Our study is, to the best of our knowledge, the first to assess the effect of two different adjuvants (AS03 and CPG/Alum) on an S-protein subunit vaccine against SARS-CoV-2 (SCB-2019), which uses Trimer-Tag technology (Clover Biopharmaceuticals, Chengdu, China) to keep the natural trimeric structure of the S-protein (S-Trimer). Immune responses to the S-Trimer protein alone (SCB-2019 with no adjuvant) were inadequate but, with both tested adjuvants (AS03 and CPG/Alum), immune responses of SCB-2019 were increased to achieve neutralising antibody titres after two vaccinations. Responses were consistent with those recorded in a panel of convalescent serum samples from patients with COVID-19. This neutralising activity directly correlates with the immune responses assessed as antibodies to the S-Trimer S-protein component and its receptor binding domain.

mRNA vaccines coding for S-protein of SARS-CoV-2 have been reported to elicit protective immune responses, based on results in clinical trials and efficacy assessments, while producing neutralising antibody titres. For stability of mRNA candidate vaccines, storage is required at less than −70°C, whereas another vaccine candidate can be stored at 2–8°C. Using proprietary technology, we created the vaccine candidate SCB-2019, which comprises S-Trimer, a trimeric form of S-protein in its natural configuration, in two adjuvanted formulations, which are stable when stored at 2–8°C, greatly facilitating distribution and use. Both SCB-2019 adjuvanted formulations were generally well tolerated and are highly immunogenic when administered as two doses 21 days apart. They elicited levels of neutralising titres comparable with those recorded in convalescent serum samples from patients with COVID-19. These findings are similar to those seen with two doses of an adjuvanted recombinant S-protein nanoparticle vaccine, supporting the rationale of this protein subunit vaccine approach. Our data support further clinical development of both SCB-2019 adjuvanted formulations."

Science: Neutralization of SARS-CoV-2 lineage B.1.1.7 pseudovirus by BNT162b2 vaccine–elicited human sera

"Recently, a new SARS-CoV-2 lineage called B.1.1.7 (variant of concern: VOC 202012/01) emerged in the United Kingdom that was reported to spread more efficiently and faster than other strains. This variant has an unusually large number of mutations with 10 amino acid changes in the spike protein, raising concerns that its recognition by neutralizing

antibodies may be affected. Here, we tested SARS-CoV-2-S pseudoviruses bearing either the Wuhan reference strain or the B.1.1.7 lineage spike protein with sera of 40 participants who were vaccinated in a previously reported trial with the mRNA-based COVID-19 vaccine BNT162b2. The immune sera had slightly reduced but overall largely preserved neutralizing titers against the B.1.1.7 lineage pseudovirus. These data indicate that the B.1.1.7 lineage will not escape BNT162b2-mediated protection."

28 January 2021

Clin Infect Dis: Bioaerosol sampling for SARS-CoV-2 in a referral center with critically ill COVID-19 patients March-May 2020

"Previous research has shown that rooms of patients with COVID-19 present the potential for healthcare-associated transmission through aerosols containing SARS-CoV-2. However, data on the presence of these aerosols outside of patient rooms are limited. We investigated whether virus-containing aerosols were present in nursing stations and patient room hallways in a referral center with critically ill COVID-19 patients.

Eight National Institute for Occupational Safety and Health BC 251 two-stage cyclone samplers were set up throughout six units, including nursing stations and visitor corridors in intensive care units and general medical units, for six hours each sampling period. Samplers were placed on tripods which held two samplers positioned 102 cm and 152 cm above the floor. Units were sampled for three days. Extracted samples underwent reverse transcription polymerase chain reaction for selected gene regions of the SARS-CoV-2 virus nucleocapsid and the housekeeping gene human RNase P as an internal control.

The units sampled varied in the number of laboratory-confirmed COVID-19 patients present on the days of sampling. Some of the units included patient rooms under negative pressure, while most were maintained at a neutral pressure. Of 528 aerosol samples collected, none were positive for SARS-CoV-2 RNA by the estimated limit of detection of 8 viral copies/m 3 of air.

Aerosolized SARS-CoV-2 outside of patient rooms was undetectable. While healthcare personnel should avoid unmasked close contact with each other, these findings may provide reassurance for the use of alternatives to tight-fitting respirators in areas outside of patient rooms during the current pandemic."

Eur J Anaesthesiol: National outcomes and characteristics of patients admitted to Swedish intensive care units for COVID-19

" To evaluate baseline characteristics, treatments and 30-day outcomes of patients admitted to Swedish ICUs with COVID-19. Admissions to Swedish ICUs from 6 March to 6

May 2020 with laboratory confirmed COVID-19 disease. The primary outcome was 30-day all-cause mortality. A multivariable model was used to determine the independent association between potential predictor variables and death.

We identified 1563 patients with complete 30-day follow-up. The 30-day all-cause mortality was 26.7%. Median age was 61 [52 to 69], Simplified Acute Physiology Score III (SAPS III) was 53 [46 to 59] and 62.5% had at least one comorbidity. Median PaO2/FiO2 on admission was 97.5 [75.0 to 140.6] mmHg, 74.7% suffered from moderate-to-severe acute respiratory failure. Age, male sex [adjusted odds ratio (aOR) 1.5 (1.1 to 2.2)], SAPS III score [aOR 1.3 (1.2 to 1.4)], severe respiratory failure [aOR 3.0 (2.0 to 4.7)], specific COVID-19 pharmacotherapy [aOR 1.4 (1.0 to 1.9)] and continuous renal replacement therapy [aOR 2.1 (1.5 to 3.0)] were associated with increased mortality. Except for chronic lung disease, the presence of comorbidities was not independently associated with mortality.

Thirty-day mortality rate in COVID-19 patients admitted to Swedish ICUs is generally lower than previously reported despite a severe degree of hypoxaemia on admission. Mortality was driven by age, baseline disease severity, the presence and degree of organ failure, rather than pre-existing comorbidities."

Obesity: COVID-19 Vaccination and Obesity: Optimism and Challenges

"Researchers have speculated that vaccines to prevent COVID-19 may be less effective for individuals with obesity, a major risk factor for mortality and morbidity from COVID-19. Initial results from the Pfizer-BioNTech and Moderna COVID-19 vaccine trials, though limited by inadequate power to compare subgroups and incomplete stratification of high-risk groups, appear to have similar efficacy among individuals with and without obesity. Careful follow up in placebo-controlled studies is required to generate data on long-term vaccine immunogenicity, particularly in high-risk groups. Subsequent analyses should stratify safety and efficacy results by each class of obesity. Speculation about variable effectiveness of COVID-19 vaccines in obesity likely increases vaccine hesitancy among individuals with obesity, who face not only a higher risk of severe outcomes from COVID-19 but also weight stigma which reduces healthcare engagement at baseline. Clinical and public health messaging must be data-driven, transparent, and sensitive to these biological and sociological vulnerabilities."

27 January 2021

Eur J Pediatr: Viral co-infections among SARS-CoV-2-infected children and infected adult household contacts

"We evaluated the rates of viral respiratory co-infections among SARS-CoV-2-infected children. Twelve percent of SARS-CoV-2-infected children had viral co-infection with one or

more common respiratory viruses. This was significantly more frequent than among their SARS-CoV-2-infected adult household contacts (0%; p=0.028). Compared to the same period the previous year, common respiratory viruses were less frequently detected (12% vs 73%, p<0.001).

Despite partial lockdown with school and daycare closure, and consequently similar exposure to common viruses between children and adults, SARS-CoV-2-infected children had more frequent viral respiratory co-infections than their SARS-CoV-2-infected adult household contacts. Circulation of common respiratory viruses was less frequent during the SARS-CoV-2 outbreak when compared to the same period last year, showing the impact of partial lockdown on the circulation of common viruses."

26 January 2021

PNAS: An evidence review of face masks against COVID-19

"The science around the use of masks by the public to impede COVID-19 transmission is advancing rapidly. In this narrative review, we develop an analytical framework to examine mask usage, synthesizing the relevant literature to inform multiple areas: population impact, transmission characteristics, source control, wearer protection, sociological considerations, and implementation considerations. A primary route of transmission of COVID-19 is via respiratory particles, and it is known to be transmissible from presymptomatic, paucisymptomatic, and asymptomatic individuals. Reducing disease spread requires two things: limiting contacts of infected individuals via physical distancing and other measures and reducing the transmission probability per contact. The preponderance of evidence indicates that mask wearing reduces transmissibility per contact by reducing transmission of infected respiratory particles in both laboratory and clinical contexts. Public mask wearing is most effective at reducing spread of the virus when compliance is high. Given the current shortages of medical masks, we recommend the adoption of public cloth mask wearing, as an effective form of source control, in conjunction with existing hygiene, distancing, and contact tracing strategies. Because many respiratory particles become smaller due to evaporation, we recommend increasing focus on a previously overlooked aspect of mask usage: mask wearing by infectious people (“source control”) with benefits at the population level, rather than only mask wearing by susceptible people, such as health care workers, with focus on individual outcomes. We recommend that public officials and governments strongly encourage the use of widespread face masks in public, including the use of appropriate regulation."

25 January 2021

Cell Rep: Cross-reactivity of SARS-CoV structural protein antibodies against SARS-CoV-2

> "In the ongoing COVID-19 pandemic, there remain unanswered questions regarding the nature and significance of the humoral immune response towards other coronavirus infections. Here, we investigate the cross-reactivity of antibodies raised against the first SARS-CoV for their reactivity towards SARS-CoV-2. We extensively characterize a selection of 10 antibodies covering all of the SARS-CoV structural proteins: spike, membrane, nucleocapsid, and envelope. While nearly all of the examined SARS-CoV antibodies displayed some level of reactivity to SARS-CoV-2, we found only partial cross-neutralization for the spike antibodies. The implications of our work are two-fold. Firstly, we have established a set of antibodies with known reactivity to both SARS-CoV and SARS-CoV-2, which will allow further study of both viruses. Secondly, we provide empirical evidence of the high propensity for antibody cross-reactivity between distinct strains of human coronaviruses, critical information for designing diagnostic and vaccine strategies for COVID-19."
>
> Preprint posted on bioRxiv on 30 July 2020

25 January 2021

Vox Sang: ABO blood group and SARS-CoV-2 antibody response in a convalescent donor population

> "ABO blood group may affect risk of SARS-CoV-2 infection and/or severity of COVID-19. We sought to determine whether IgG, IgA and neutralizing antibody (nAb) to SARS-CoV-2 vary by ABO blood group.
>
> Among eligible convalescent plasma donors, ABO blood group was determined via agglutination of reagent A1 and B cells, IgA and IgG were quantified using the Euroimmun anti-SARS-CoV-2 ELISA, and nAb titres were quantified using a microneutralization assay. Differences in titre distribution were examined by ABO blood group using non-parametric Kruskal–Wallis tests. Adjusted prevalence ratios (aPR) of high nAb titre (≥1:160) were estimated by blood group using multivariable modified Poisson regression models that adjusted for age, sex, hospitalization status and time since SARS-CoV-2 diagnosis.
>
> Of the 202 potential donors, 65 (32%) were blood group A, 39 (19%) were group B, 13 (6%) were group AB, and 85 (42%) were group O. Distribution of nAb titres significantly differed by ABO blood group, whereas there were no significant differences in anti-spike IgA or anti-spike IgG titres by ABO blood group. There were significantly more individuals with high nAb titre (≥1:160) among those with blood group B, compared with group O (aPR = 1·9 [95%CI =

1·1–3·3], P = 0·029). Fewer individuals had a high nAb titre among those with blood group A, compared with group B (aPR = 0·6 [95%CI = 0·4-1·0], P = 0·053).

Eligible CCP donors with blood group B may have relatively higher neutralizing antibody titres. Additional studies evaluating ABO blood groups and antibody titres that incorporate COVID-19 severity are needed."

22 January 2021

Acad Emerg Med: SARS-CoV-2 viral load in nasopharyngeal swabs in the ED does not predict COVID-19 severity and mortality

"The ongoing COVID-19 pandemic has led to devastating repercussions on health care systems worldwide. This viral infection has a broad clinical spectrum broad (ranging from influenza-like disease, viral pneumonia, and hypoxemia to acute respiratory distress syndrome requiring prolonged intensive care unit stays). The prognostic impact of measuring viral load on nasopharyngeal swab specimens (by reverse transcriptase polymerase chain reaction [RT-PCR]) is yet to be elucidated.

Between March 3 and April 5, 2020, we conducted a retrospective study on a cohort of COVID-19 patients (mild or severe disease) who were hospitalized after presenting to the emergency department (ED) and had at least one positive nasopharyngeal swab during their hospital stay. We led our study at the University Hospitals of Strasbourg in the Greater East region of France, one of the pandemic's epicenters in Europe.

We have collected samples from a cohort of 287 patients with a confirmed diagnosis of COVID-19 who were included in our study. Nearly half of them (50.5%) presented a mild form of the disease, while the other half (49.5%) presented a severe form, requiring mechanical ventilation. Median (interquartile range) viral load on the initial upper respiratory swab at admission was 4.76 (3.29–6.06) log10 copies/reaction. When comparing survivors and nonsurvivors, this viral load measurement did not differ according to subgroups (p = 0.332). Additionally, we have found that respiratory viral load measurement was predictive of neither in-hospital mortality (adjusted odds ratio [AOR] = 1.05, 95% confidence interval [CI] = 0.85 to 1.31, p = 0.637) nor disease severity (AOR = 0.88, 95% CI = 0.73 to 1.06, p = 0.167).

Respiratory viral load measurement on the first nasopharyngeal swab (by RT-PCR) during initial ED management is neither a predictor of severity nor a predictor of mortality in SARS-CoV-2 infection. Host response to this viral infection along with the extent of preexisting comorbidities might be more foretelling of disease severity than the virus itself."

Circulation: Microthrombi As A Major Cause of Cardiac Injury in COVID-19: A Pathologic Study

"Background: Cardiac injury is common in hospitalized patients with COVID-19 and portends poorer prognosis. However, the mechanism and the type of myocardial damage associated with SARS-CoV-2 remain uncertain.

Methods: We conducted a systematic pathologic analysis of 40 hearts from hospitalized patients dying of Coronavirus Disease 2019 (COVID-19) in Bergamo, Italy to determine the pathologic mechanisms of cardiac injury. We divided the hearts according to presence or absence of acute myocyte necrosis and then determined the underlying mechanisms of cardiac injury.

Results: Of the 40 hearts examined, 14 (35%) had evidence of myocyte necrosis, predominantly of the left ventricle. As compared to subjects without necrosis, subjects with necrosis tended to be female, have chronic kidney disease, and shorter symptom onset to admission. The incidence of severe coronary artery disease (i.e., >75% cross sectional narrowing) was not significantly different between those with and without necrosis. 3/14 (21 .4%) subjects with myocyte necrosis showed evidence of acute myocardial infarction defined as ≥1 cm2 area of necrosis while 11/14 (78.6%) showed evidence of focal (> 20 necrotic myocytes with an area of ≥ 0.05 mm2 but <1 cm2) myocyte necrosis. Cardiac thrombi were present in 11/14 (78.6%) cases with necrosis, with 2/14 (14.2%) having epicardial coronary artery thrombi while 9/14 (64.3%) had microthrombi in myocardial capillaries, arterioles, and small muscular arteries.

We compared cardiac microthrombi from COVID-19 positive autopsy cases to intramyocardial thromboemboli from COVID-19 cases as well as to aspirated thrombi obtained during primary percutaneous coronary intervention from uninfected and COVID-19 infected patients presenting with ST-segment elevation myocardial infarction (STEMI). Microthrombi had significantly greater fibrin and terminal complement C5b-9 immunostaining as compared to intramyocardial thromboemboli from COVID-19 negative subjects and to aspirated thrombi. There were no significant differences between the constituents of thrombi aspirated from COVID-19 positive and negative STEMI patients.

Conclusions: The most common pathologic cause of myocyte necrosis was microthrombi. Microthrombi were different in composition as compared to intramyocardial thromboemboli from COVID-19 negative subjects and to coronary thrombi retrieved from COVID-19 positive and negative STEMI patients. Tailored anti-thrombotic strategies may be useful to counteract the cardiac effects of COVID-19 infection."

ICYMI (older than the last 2 weeks)

J Diabetes Sci Technol: How to Best Protect People With Diabetes From the Impact of SARS-CoV-2: Report of the International COVID-19 and Diabetes Summit (21 January 2021)

> "The coronavirus disease 2019 (COVID-19) pandemic caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus has rapidly involved the entire world and exposed the pressing need for collaboration between public health and other stakeholders from the clinical, scientific, regulatory, pharmaceutical, and medical device and technology communities. To discuss how to best protect people with diabetes from serious outcomes from COVID-19, Diabetes Technology Society, in collaboration with Sansum Diabetes Research Institute, hosted the "International COVID-19 and Diabetes Virtual Summit" on August 26-27, 2020. This unique, unprecedented real-time conference brought together physicians, scientists, government officials, regulatory experts, industry representatives, and people with diabetes from six continents to review and analyze relationships between COVID-19 and diabetes…. While there was an emphasis on diabetes and its interactions with COVID-19, the panelists also discussed the COVID-19 pandemic in general. The meeting generated many novel ideas for collaboration between experts in medicine, science, government, and industry to develop new technologies and disease treatment paradigms to fight this global pandemic."

J Clin Microbiol: A systematic review and meta-analysis of upper airways swab collection for detection of viral and bacterial pathogens by individuals or caregivers compared to healthcare workers (19 January 2021)

> "Self- or caregiver-collection of upper airway swabs reduces infectious exposures of healthcare workers (HCW) and the need to redeploy clinical staff to testing roles. We aimed to determine whether self- or caregiver-collection has adequate diagnostic performance for detection of viral and bacterial upper airways pathogens.
>
> We did a systematic review and meta-analysis of studies comparing diagnostic accuracy of self- or caregiver-collected upper airway swabs collected by patients or caregivers compared to HCW. All study types except case reports and series were included if sufficient data were presented to calculate sensitivity, specificity and Cohen's kappa. Studies published from 1946 to 17th August 2020 were included in the search. We did a meta-analysis to assess pooled sensitivity and specificity.
>
> Twenty studies were included in the systematic review and 15 in the meta-analysis. Overall sensitivity of swabs collected by patients or caregivers compared to HCW was 91% (95% CI: 87-94) and specificity was 98% (95% CI: 96-99). Sensitivity ranged from 65% to 100% and specificity from 73% to 100% across the studies. All but one study concluded that self- or caregiver-collected swabs were acceptable for detection of upper airway pathogens.

> Self- and caregiver-collection of upper airway swabs had reassuring diagnostic performance for multiple pathogens. There are numerous potential benefits of self- and caregiver-collected swabs for patients, families, researchers, and health systems. Further research to optimize implementation of sample collection by patients and caregivers is warranted."

Alzheimers Dement: The chronic neuropsychiatric sequelae of COVID-19: The need for a prospective study of viral impact on brain functioning (05 January 2021)

> "The increasing evidence of SARS-CoV-2 impact on the central nervous system (CNS) raises key questions on its impact for risk of later life cognitive decline, Alzheimer's disease (AD), and other dementia.
>
> The Alzheimer's Association and representatives from more than 30 countries—with technical guidance from the World Health Organization—have formed an international consortium to study the short-and long-term consequences of SARS-CoV-2 on the CNS—including the underlying biology that may contribute to AD and other dementias. This consortium will link teams from around the world covering more than 22 million COVID-19 cases to enroll two groups of individuals including people with disease, to be evaluated for follow-up evaluations at 6, 9, and 18 months, and people who are already enrolled in existing international research studies to add additional measures and markers of their underlying biology.
>
> The increasing evidence and understanding of SARS-CoV-2's impact on the CNS raises key questions on the impact for risk of later life cognitive decline, AD, and other dementia. This program of studies aims to better understand the long-term consequences that may impact the brain, cognition, and functioning—including the underlying biology that may contribute to AD and other dementias."

Emerg Infect Dis: Addressing COVID-19 Misinformation on Social Media Preemptively and Responsively (04 January 2021)

> "Efforts to address misinformation on social media have special urgency with the emergence of coronavirus disease (COVID-19). In one effort, the World Health Organization (WHO) designed and publicized shareable infographics to debunk coronavirus myths. We used an experiment to test the efficacy of these infographics, depending on placement and source. We found that exposure to a corrective graphic on social media reduced misperceptions about the science of 1 false COVID-19 prevention strategy but did not affect misperceptions about prevention of COVID-19. Lowered misperceptions about the science persisted >1 week later. These effects were consistent when the graphic was shared by the World Health Organization or by an anonymous Facebook user and when the graphics were shared preemptively or in response to misinformation. Health organizations can and should create and promote shareable graphics to improve public knowledge."

Thromb Haemost: Heparin Inhibits Cellular Invasion by SARS-CoV-2: Structural Dependence of the Interaction of the Spike S1 Receptor-Binding Domain with Heparin (23 December 2020)

> "The dependence of development and homeostasis in animals on the interaction of hundreds of extracellular regulatory proteins with the peri- and extracellular glycosaminoglycan heparan sulfate (HS) is exploited by many microbial pathogens as a means of adherence and invasion. Heparin, a widely used anticoagulant drug, is structurally similar to HS and is a common experimental proxy. Exogenous heparin prevents infection by a range of viruses, including S-associated coronavirus isolate HSR1. Here, we show that heparin inhibits severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) invasion of Vero cells by up to 80% at doses achievable through prophylaxis and, particularly relevant, within the range deliverable by nebulisation. Surface plasmon resonance and circular dichroism spectroscopy demonstrate that heparin and enoxaparin, a low-molecular-weight heparin which is a clinical anticoagulant, bind and induce a conformational change in the spike (S1) protein receptor-binding domain (S1 RBD) of SARS-CoV-2. A library of heparin derivatives and size-defined fragments were used to probe the structural basis of this interaction. Binding to the RBD is more strongly dependent on the presence of 2-O or 6-O sulfate groups than on N-sulfation and a hexasaccharide is the minimum size required for secondary structural changes to be induced in the RBD. It is likely that inhibition of viral infection arises from an overlap between the binding sites of heparin/HS on S1 RBD and that of the angiotensin-converting enzyme 2. The results suggest a route for the rapid development of a first-line therapeutic by repurposing heparin and its derivatives as antiviral agents against SARS-CoV-2 and other members of the *Coronaviridae*."

Selected Literature: Preprints

Preprints are found on preprint servers such as arXiv, bioRxiv, and medRxiv; they are commonly used for biomedical research. Preprints may later be published in peer-reviewed journals. Per medRxiv: "Preprints are preliminary reports of work that have not been certified by peer review. They should not be relied on to guide clinical practice or health-related behavior and should not be reported in news media as established information."

medRxiv: SARS-CoV-2 B.1.1.7 escape from mRNA vaccine-elicited neutralizing antibodies (03 February 2021)

> "SARS-CoV-2 transmission is uncontrolled in many parts of the world, compounded in some areas by higher transmission potential of the B1.1.7 variant now seen in 50 countries. It is unclear whether responses to SARS-CoV-2 vaccines based on the prototypic strain will be impacted by mutations found in B.1.1.7. Here we assessed immune responses following

vaccination with mRNA-based vaccine BNT162b2. We measured neutralising antibody responses following a single immunization using pseudoviruses expressing the wild-type Spike protein or the 8 mutations found in the B.1.1.7 Spike protein. The vaccine sera exhibited a broad range of neutralizing titres against the wild-type pseudoviruses that were modestly reduced against B.1.1.7 variant. This reduction was also evident in sera from some convalescent patients. Decreased B.1.1.7 neutralization was also observed with monoclonal antibodies targeting the N-terminal domain (9 out of 10), the Receptor Binding Motif (RBM) (5 outof 29), but not in neutralizing mAbs binding outside the RBM. Introduction of the E484K mutation in a B.1.1.7 background to reflect newly emerging viruses in the UK led to a more substantial loss of neutralizing activity by vaccine-elicited antibodies over that conferred by the B.1.1.7 mutations alone. Further work is needed to establish the impact of these observations on protective vaccine efficacy in the context of the evolving B.1.1.7 lineage."

medRxiv: Robust spike antibody responses and increased reactogenicity in seropositive individuals after a single dose of SARS-CoV-2 mRNA vaccine (posted 01 February 2021)

"An important question is arising as COVID-19 vaccines are getting rolled out: Should individuals who already had a SARS-CoV-2 infection receive one or two shots of the currently authorized mRNA vaccines. In this short report, we show that the antibody response to the first vaccine dose in individuals with pre-existing immunity is equal to or even exceeds the titers found in naïve individuals after the second dose. We also show that the reactogenicity is significantly higher in individuals who have been infected with SARS-CoV-2 in the past. Changing the policy to give these individuals only one dose of vaccine would not negatively impact on their antibody titers, spare them from unnecessary pain and free up many urgently needed vaccine doses."

SSRN: Single Dose Administration, And The Influence Of The Timing Of The Booster Dose On Immunogenicity and Efficacy Of ChAdOx1 nCoV-19 (AZD1222) Vaccine (posted 01 February 2021)

"The ChAdOx1 nCoV-19 (AZD1222) vaccine has been approved for emergency use by the UK regulatory authority, MHRA, with a regimen of two standard doses given with an interval of between 4 and 12 weeks. The planned rollout in the UK will involve vaccinating people in high risk categories with their first dose immediately, and delivering the second dose 12 weeks later.Here we provide both a further prespecified pooled analysis of trials of ChAdOx1 nCoV-19 and exploratory analyses of the impact on immunogenicity and efficacy of extending the interval between priming and booster doses. In addition, we show the immunogenicity and protection afforded by the first dose, before a booster dose has been offered.

We present data from phase III efficacy trials of ChAdOx1 nCoV-19 in the United Kingdom and Brazil, and phase I/II clinical trials in the UK and South Africa, against symptomatic disease caused by SARS-CoV-2. The data cut-off date for these analyses was 7th December 2020. The accumulated cases of COVID-19 disease at this cut-off date exceeds the number required for a pre-specified final analysis, which is also presented. As previously described, individuals over 18 years of age were randomised 1:1 to receive two standard doses (SD) of ChAdOx1 nCoV-19 (5x1010 viral particles) or a control vaccine/saline placebo. In the UK trial efficacy cohort a subset of participants received a lower dose (LD, 2.2x1010 viral particles) of the ChAdOx1 nCoV-19 for the first dose. All cases with a nucleic acid amplification test (NAAT) were adjudicated for inclusion in the analysis, by a blinded independent endpoint review committee. Studies are registered at ISRCTN89951424 and ClinicalTrials.gov; NCT04324606, NCT04400838, and NCT04444674.

17,177 baseline seronegative trial participants were eligible for inclusion in the efficacy analysis, 8948 in the UK, 6753 in Brazil and 1476 in South Africa, with 619 documented NAAT +ve infections of which 332 met the primary endpoint of symptomatic infection >14 days post dose 2.The primary analysis of overall vaccine efficacy >14 days after the second dose including LD/SD and SD/SD groups, based on the prespecified criteria was 66.7% (57.4%, 74.0%). There were no hospitalisations in the ChAdOx1 nCoV-19 group after the initial 21 day exclusion period, and 15 in the control group.Vaccine efficacy after a single standard dose of vaccine from day 22 to day 90 post vaccination was 76% (59%, 86%), and modelled analysis indicated that protection did not wane during this initial 3 month period. Similarly, antibody levels were maintained during this period with minimal waning by day 90 day (GMR 0.66, 95% CI 0.59, 0.74).In the SD/SD group, after the second dose, efficacy was higher with a longer prime-boost interval: VE 82.4% 95%CI 62.7%, 91.7% at 12+ weeks, compared with VE 54.9%, 95%CI 32.7%, 69.7% at <6 weeks. These observations are supported by immunogenicity data which showed binding antibody responses more than 2-fold higher after an interval of 12 or more weeks compared with and interval of less than 6 weeks GMR 2.19 (2.12, 2.26) in those who were 18-55 years of age.

ChAdOx1 nCoV-19 vaccination programmes aimed at vaccinating a large proportion of the population with a single dose, with a second dose given after a 3 month period is an effective strategy for reducing disease, and may be the optimal for rollout of a pandemic vaccine when supplies are limited in the short term."

bioRxiv: E484K as an innovative phylogenetic event for viral evolution: Genomic analysis of the E484K spike mutation in SARS-CoV-2 lineages from Brazil (posted 27 January 2021)

"The COVID-19 pandemic caused by SARS-CoV-2 has affected millions of people since its beginning in 2019. The propagation of new lineages and the discovery of key mechanisms adopted by the virus to overlap the immune system are central topics for the entire public health policies, research and disease management. Since the second semester 2020, the

mutation E484K has been progressively found in the Brazilian territory, composing different lineages over time. It brought multiple concerns related to the risk of reinfection and the effectiveness of new preventive and treatment strategies due to the possibility of escaping from neutralizing antibodies. To better characterize the current scenario we performed genomic and phylogenetic analyses of the E484K mutated genomes sequenced from Brazilian samples in 2020. From October, 2020, 43.9% of the sequenced genomes present the E484K mutation, which was identified in three different lineages (P1, P2 and B.1.1.33) in four Brazilian regions. We also evaluated the presence of E484K associated mutations and identified selective pressures acting on the spike protein, leading us to some insights about adaptive and purifying selection driving the virus evolution."

bioRxiv: Publication practices during the COVID-19 pandemic: Biomedical preprints and peer-reviewed literature (posted 21 January 2021)

"The coronavirus pandemic introduced many changes to our society, and deeply affected the established in biomedical sciences publication practices. In this article, we present a comprehensive study of the changes in scholarly publication landscape for biomedical sciences during the COVID-19 pandemic, with special emphasis on preprints posted on bioRxiv and medRxiv servers. We observe the emergence of a new category of preprint authors working in the fields of immunology, microbiology, infectious diseases, and epidemiology, who extensively used preprint platforms during the pandemic for sharing their immediate findings. The majority of these findings were works-in-progress unfitting for a prompt acceptance by refereed journals. The COVID-19 preprints that became peer-reviewed journal articles were often submitted to journals concurrently with the posting on a preprint server, and the entire publication cycle, from preprint to the online journal article, took on average 63 days. This included an expedited peer-review process of 43 days and journal's production stage of 15 days, however there was a wide variation in publication delays between journals. Only one third of COVID-19 preprints posted during the first nine months of the pandemic appeared as peer-reviewed journal articles. These journal articles display high Altmetric Attention Scores further emphasizing a significance of COVID-19 research during 2020. This article will be relevant to editors, publishers, open science enthusiasts, and anyone interested in changes that the 2020 crisis transpired to publication practices and a culture of preprints in life sciences."

News in Brief

The volunteer-driven COVID Tracking Project, which has been compiling, publishing, and interpreting vital COVID-19 data, will stop its work in March. They write: "But the work itself—compiling, cleaning, standardizing, and making sense of COVID-19 data from 56 individual states and territories—is properly the work of federal public health agencies" (COVID TP).

Podcast: "Fixing the world's pandemic alarm. A year ago the WHO's coronavirus emergency alarm was largely ignored. Why?" (Nature)

"How to better read COVID-19 data: Pandemic data can be difficult to parse and weigh. In today's newsletter, two experts offer five tips for improving your COVID-19 data literacy" (Atlantic).

The New Variants

"The most worrying mutations in five emerging coronavirus variants: Here is a guide to novel versions of the COVID-causing virus—and genetic changes that can make them more contagious and evasive in the body" (SciAm).

If you are more visual and/or think better with Legos… "What's going on with all these coronavirus variants? An illustrated guide" (NPR).

A case of COVID-19 with the South Africa variant has been identified in Maryland—an adult in the Baltimore metro region with no history of international travel (Maryland.gov).

According to Dr. Fauci, with the new variants in circulation, there is a 'very high rate of reinfection' possible (CNN).

Transmission, Testing, and Mitigation Measures

Fewer people are getting tested for COVID-19, and that's a problem (Atlantic).

Rapid, at-home coronavirus testing should be available later this year (WashPo).

"COVID-19 rarely spreads through surfaces. So why are we still deep cleaning?" (Nature)

Vaccines

Johnson & Johnson has applied for an EUA for its single-shot COVID-19 vaccine (J&J).

British researchers are looking at a mix-and-match COVID vaccine dosing strategy in a new study out of Oxford (COM-COV).

"How to redesign COVID vaccines so they protect against variants" (Nature).

Anti-vax protestors temporary delayed vaccination efforts in Los Angeles (NPR).

An interim data analysis suggests that Russia's Sputnik V COVID-19 vaccine is 92% effective (BBC; see also: article in The Lancet, noted above).

"Germany is ordering vaccines for 2022 in case regular or booster doses are needed to keep the population immune against variants of COVID-19" (Reuters).

Previous administration officials lobbied Congress to deny funding to states for vaccine support (STAT).

Vaccines – Who's Getting Them?

"Why aren't more health-care workers getting vaccinated?" (NYMag).

The health disparities continue—Black and Hispanic Americans aren't getting COVID-19 vaccinations at the same rate as whites (Reuters).

Tanzania's health ministry 'has no plans to receive vaccines for COVID-19'; the president has asserted that God eliminated COVID-19 in Tanzania and the country has not updated their infection data since April (AP).

"More than 85 poor countries will not have widespread access to coronavirus vaccines before 2023" (EIU).

If you travel, a vaccine passport might be in your future (NYT).

Thanks, Coronavirus

Researchers are using huge data sets to track surges in mental health disorders like depression linked to the pandemic (Nature).

Researchers aren't sure of the connection, but they are seeing new onset of diabetes with COVID-19 cases (WashPo; see also: article from Diabetes Obes Metab published 27 Nov 2020).

From bureaucratic paperwork pileups of death certificates to shortages in caskets, the death care industry is under strain during the pandemic (Post-Gazette).

Long Reads

"What went wrong with America's $44 million vaccine data system? The CDC ordered software that was meant to manage the vaccine rollout. Instead, it has been plagued by problems and abandoned by most states" (MIT Tech Rev).

This one isn't specific to COVID or even the pandemic, but it is striking: "Nitrous nation: Hippie crack. Whippets. Laughing gas. A casual party drug endures." (NYT).

Other Outbreaks and Infectious Diseases

"The pandemic broke the flu: This winter has been an extraordinarily quiet flu season. Scientists aren't sure the silence will last" (Atlantic).

The CDC is investigating a multistate, food-sourced outbreak of *Escherichia coli* O157:H7; the source is currently unknown (CDC).

Pandemic distancing and masking are being credited for fewer cases of acute flaccid myelitis that develops in some children with enterovirus infections (STAT).

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